

Claims:

1. A GLP-1 compound comprising a GLP-1 peptide modified with a reactive group that reacts with a thiol group on a blood component to form a covalent bond, wherein said reactive group is selected from the group consisting of an activated disulfide bond group or an S-sulfonate.
2. The GLP-1 compound of claim 1, said GLP-1 peptide having the amino acid sequence of formula 1 (SEQ ID NO:1)

Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Lys-Gly-Arg-Xaa₃₇

Formula 1 (SEQ ID NO: 1)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu;

Xaa₃₃ is: Val, or Ile;

Xaa₃₇ is: L-Cys, D-Cys, homocysteine, or penicillamine;

wherein said GLP-1 peptide is modified at Xaa₃₇; and

provided that the GLP-1 compound does not have the sequence of GLP-1(7-37)OH, GLP-1(7-36)-NH₂, Gly⁸-GLP-1(7-37)OH, Gly⁸-GLP-1(7-36)NH₂, Val⁸-

GLP-1(7-37)OH, Val⁸-GLP-1(7-36)NH₂, Leu⁸-GLP-1(7-37)OH, Leu⁸-GLP-1(7-36)NH₂, Ile⁸-GLP-1(7-37)OH, Ile⁸-GLP-1(7-36)NH₂, Ser⁸-GLP-1(7-37)OH, Ser⁸-GLP-1(7-36)NH₂, Thr⁸-GLP-1(7-37)OH, Thr⁸-GLP-1(7-36)NH₂, Val⁸-Tyr¹²-GLP-1(7-37)OH, Val⁸-Tyr¹²-GLP-1(7-36)NH₂, Val⁸-Tyr¹⁶-GLP-1(7-37)OH, Val⁸-Tyr¹⁶-GLP-1(7-36)NH₂, Val⁸-Glu²²-GLP-1(7-37)OH, Val⁸-Glu²²-GLP-1(7-36)NH₂, Gly⁸-Glu²²-GLP-1(7-37)OH, Gly⁸-Glu²²-GLP-1(7-36)NH₂, Val⁸-Asp²²-GLP-1(7-37)OH, Val⁸-Asp²²-GLP-1(7-36)NH₂, Gly⁸-Asp²²-GLP-1(7-37)OH, Gly⁸-Asp²²-GLP-1(7-36)NH₂, Gly⁸-Lys²²-GLP-1(7-37)OH, Gly⁸-Lys²²-GLP-1(7-36)NH₂, Leu⁸-Glu²²-GLP-1(7-37)OH, Leu⁸-Glu²²-GLP-1(7-36)NH₂, Ile⁸-Glu²²-GLP-1(7-37)OH, Ile⁸-Glu²²-GLP-1(7-36)NH₂, Leu⁸-Asp²²-GLP-1(7-37)OH, Leu⁸-Asp²²-GLP-1(7-36)NH₂, Ile⁸-Asp²²-GLP-1(7-37)OH, Ile⁸-Asp²²-GLP-1(7-36)NH₂, Leu⁸-Lys²²-GLP-1(7-37)OH, Leu⁸-Lys²²-GLP-1(7-36)NH₂, Ile⁸-Lys²²-GLP-1(7-37)OH, Ile⁸-Lys²²-GLP-1(7-36)NH₂, Ser⁸-Glu²²-GLP-1(7-37)OH, Ser⁸-Glu²²-GLP-1(7-36)NH₂, Ser⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Asp²²-GLP-1(7-36)NH₂, Thr⁸-Asp²²-GLP-1(7-37)OH, Thr⁸-Asp²²-GLP-1(7-36)NH₂, Ser⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Asp²²-GLP-1(7-36)NH₂, Thr⁸-Glu²²-GLP-1(7-37)OH, Thr⁸-Glu²²-GLP-1(7-36)NH₂, Ser⁸-Glu²²-GLP-1(7-37)OH, Ser⁸-Glu²²-GLP-1(7-36)NH₂, Thr⁸-Asp²²-GLP-1(7-37)OH, Thr⁸-Asp²²-GLP-1(7-36)NH₂, Ser⁸-Lys²²-GLP-1(7-37)OH, Ser⁸-Lys²²-GLP-1(7-36)NH₂, Leu⁸-Glu²²-GLP-1(7-37)OH, Leu⁸-Glu²²-GLP-1(7-36)NH₂, Ile⁸-Glu²²-GLP-1(7-37)OH, Ile⁸-Glu²²-GLP-1(7-36)NH₂, Asp²²-GLP-1(7-37)OH, Asp²²-GLP-1(7-36)NH₂, Lys²²-GLP-1(7-37)OH, Lys²²-GLP-1(7-36)NH₂, Val⁸-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu²²-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-36)NH₂, Gly⁸-Glu³⁰-GLP-1(7-37)OH, Gly⁸-Glu³⁰-GLP-1(7-36)NH₂, Leu⁸-Glu³⁰-GLP-1(7-37)OH, Leu⁸-Glu³⁰-GLP-1(7-36)NH₂, Ile⁸-Glu³⁰-GLP-1(7-37)OH, Ile⁸-Glu³⁰-GLP-1(7-36)NH₂, Ser⁸-Glu³⁰-GLP-1(7-37)OH, Ser⁸-Glu³⁰-GLP-1(7-36)NH₂, Thr⁸-Glu³⁰-GLP-1(7-37)OH, Thr⁸-Glu³⁰-GLP-1(7-36)NH₂, Val⁸-His³⁷-GLP-1(7-37)OH, Val⁸-His³⁷-GLP-1(7-36)NH₂, Gly⁸-His³⁷-GLP-1(7-37)OH, Gly⁸-His³⁷-GLP-1(7-36)NH₂, Leu⁸-His³⁷-GLP-1(7-37)OH, Leu⁸-His³⁷-GLP-1(7-36)NH₂, Ser⁸-His³⁷-GLP-1(7-37)OH, Ser⁸-His³⁷-GLP-1(7-36)NH₂, Thr⁸-His³⁷-GLP-1(7-37)OH, Thr⁸-His³⁷-GLP-1(7-36)NH₂.

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3. The GLP-1 compound of claim 1, said GLP-1 peptide having the amino acid sequence of formula 2 (SEQ ID NO:2)

Xaa₇-Xaa₈-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Tyr-Leu-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Xaa₃₃-Lys-Gly-Arg-Xaa₃₇

Formula 2 (SEQ ID NO:2)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Gly, Ala, Val, Leu, Ile, Ser, or Thr;

Xaa₁₆ is: Val, Phe, Tyr, or Trp;

Xaa₁₈ is: Ser, Tyr, Trp, Phe, Lys, Ile, Leu, or Val;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₃₃ is: Val or Ile; and

Xaa₃₇ is: L-Cys, D-Cys, homocysteine, or penicillamine;

wherein said GLP-1 peptide is modified at Xaa₃₇; and

provided that the GLP-1 compound does not have the sequence of GLP-1(7-37)OH, GLP-1(7-36)-NH₂, Gly⁸-GLP-1(7-37)OH, Gly⁸-GLP-1(7-36)NH₂, Val⁸-GLP-1(7-37)OH, Val⁸-GLP-1(7-36)NH₂, Leu⁸-GLP-1(7-37)OH, Leu⁸-GLP-1(7-36)NH₂, Ile⁸-GLP-1(7-37)OH, Ile⁸-GLP-1(7-36)NH₂, Ser⁸-GLP-1(7-37)OH, Ser⁸-GLP-1(7-36)NH₂, Thr⁸-GLP-1(7-37)OH, Thr⁸-GLP-1(7-36)NH₂, Val⁸-Tyr¹⁶-GLP-1(7-37)OH, Val⁸-Tyr¹⁶-GLP-1(7-36)NH₂, Val⁸-Glu²²-GLP-1(7-37)OH, Val⁸-Glu²²-GLP-1(7-36)NH₂, Gly⁸-Glu²²-GLP-1(7-37)OH, Gly⁸-Glu²²-GLP-1(7-36)NH₂, Val⁸-Asp²²-GLP-1(7-37)OH, Val⁸-Asp²²-GLP-1(7-36)NH₂, Gly⁸-Asp²²-GLP-1(7-37)OH, Gly⁸-Asp²²-GLP-1(7-36)NH₂, Val⁸-Lys²²-GLP-1(7-36)NH₂, Gly⁸-Lys²²-GLP-1(7-36)NH₂, Leu⁸-Glu²²-GLP-1(7-37)OH, Leu⁸-Glu²²-GLP-1(7-36)NH₂, Ile⁸-Glu²²-GLP-1(7-36)NH₂, Leu⁸-Asp²²-GLP-1(7-37)OH, Ile⁸-Asp²²-GLP-1(7-36)NH₂, Ile⁸-Asp²²-GLP-1(7-37)OH, Ile⁸-Asp²²-GLP-1(7-36)NH₂, Leu⁸-Lys²²-GLP-1(7-37)OH, Leu⁸-Lys²²-GLP-1(7-36)NH₂, Ile⁸-Lys²²-

GLP-1(7-37)OH, Ile⁸-Lys²²-GLP-1(7-36)NH₂, Ser⁸-Glu²²-GLP-1(7-37)OH, Ser⁸-Glu²²-GLP-1(7-36)NH₂, Thr⁸-Glu²²-GLP-1(7-37)OH, Thr⁸-Glu²²-GLP-1(7-36)NH₂, Ser⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Asp²²-GLP-1(7-36)NH₂, Thr⁸-Asp²²-GLP-1(7-37)OH, Thr⁸-Asp²²-GLP-1(7-36)NH₂, Ser⁸-Lys²²-GLP-1(7-37)OH, Ser⁸-Lys²²-GLP-1(7-36)NH₂, Thr⁸-Lys²²-GLP-1(7-37)OH, Thr⁸-Lys²²-GLP-1(7-36)NH₂, Glu²²-GLP-1(7-37)OH, Glu²²-GLP-1(7-36)NH₂, Asp²²-GLP-1(7-37)OH, Asp²²-GLP-1(7-36)NH₂, Lys²²-GLP-1(7-37)OH, Lys²²-GLP-1(7-36)NH₂.

4. The GLP-1 compound of claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 3 (SEQ ID NO:3)

Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈

Formula 3 (SEQ ID NO:3)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu;

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, Ser, L-Cys, D-Cys, homocysteine, or penicillamine;
 Xaa₃₈ is: Ser, Pro, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂;
 Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₀ is: Ser, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₂ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₃ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₄ is: Pro, Ala, Arg, Lys, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₅ is: Ser, His, Pro, Lys, Arg, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₆ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 Xaa₄₇ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; and
 Xaa₄₈ is: L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
 wherein said extended GLP-1 peptide contains a single L-Cys, D-Cys, homocysteine, or penicillamine which occurs at one of Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, or Xaa₄₈, said GLP-1 is modified at said single L-Cys, D-Cys, homocysteine, or penicillamine; and
 provided that if Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent and further provided that the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₆: Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Ser-NH₂.

5. The GLP-1 compound of claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 4 (SEQ ID NO:4)

Xaa₇-Xaa₈-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Xaa₁₆-Ser-Ser-Tyr-Lys-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-

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Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-
Xaa₄₇-Xaa₄₈

Formula 4 (SEQ ID NO: 4)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, Ser, L-Cys, D-Cys, homocysteine, or penicillamine;

Xaa₃₈ is: Ser, Pro, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₀ is: Ser, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₂ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; and

Xaa₄₈ is: L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

wherein said extended GLP-1 peptide contains a single L-Cys, D-Cys, homocysteine, or penicillamine which occurs at one of Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, or Xaa₄₈, said GLP-1 is modified at said single L-Cys, D-Cys, homocysteine, or penicillamine; and provided that if Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent and further provided that the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₆: Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH₂.

6. The GLP-1 compound of claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 5 (SEQ ID NO:5)

Xaa₇-Xaa₈-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Lys-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Xaa₃₃-Lys-Gly-Gly-Pro-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈

Formula 5 (SEQ ID NO:5)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₃₃ is: Val or Ile;

Xaa₃₈ is: Ser, Pro, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₀ is: Ser, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₂ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; and

Xaa₄₈ is: L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; wherein said extended GLP-1 peptide contains a single L-Cys, D-Cys, homocysteine, or penicillamine which occurs at one of Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, or Xaa₄₈, said GLP-1 is modified at said single L-Cys, D-Cys, homocysteine, or penicillamine; and provided that if Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent.

7. The GLP-1 compound of claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 6 (SEQ ID NO:6)
- Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈-Xaa₄₉-Xaa₅₀-Xaa₅₁

Formula 6 (SEQ ID NO:6)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;
Xaa₂₅ is: Ala, Val, Ile, or Leu;
Xaa₂₇ is: Glu, Ile, or Ala;
Xaa₃₀ is: Ala or Glu
Xaa₃₃ is: Val or Ile;
Xaa₃₄ is: Lys, Asp, Arg, or Glu;
Xaa₃₆ is: Gly, Pro, or Arg;
Xaa₃₇ is: Gly, Pro, or Ser;
Xaa₃₈ is: Ser, Pro, or His;
Xaa₃₉ is: Ser, Arg, Thr, Trp, or Lys;
Xaa₄₀ is: Ser or Gly;
Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, or Gly;
Xaa₄₂ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
Xaa₄₃ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, L-Cys, D-Cys, homocysteine, penicillamine, NH₂,
or is absent;
Xaa₄₅ is: Ser, His, Pro, Lys, Arg, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂,
or is absent;
Xaa₄₆ is: His, Ser, Arg, Lys, Pro, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂,
or is absent;
Xaa₄₇ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is
absent;
Xaa₄₈ is: Gly, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
Xaa₄₉ is: Pro, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
Xaa₅₀ is: Ser, His, Ser-NH₂, His-NH₂, L-Cys, D-Cys, homocysteine, penicillamine, NH₂,
or is absent; and
Xaa₅₁ is: L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;
wherein said extended GLP-1 peptide contains a single L-Cys, D-Cys, homocysteine, or
penicillamine which occurs at one of Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈,
Xaa₄₉, Xaa₅₀, or Xaa₅₁ said GLP-1 is modified at said single L-Cys, D-Cys, homocysteine,

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or penicillamine; and provided that if Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, or Xaa₅₀, is absent each amino acid downstream is absent and further provided that if Xaa₃₆ is Arg and Xaa₃₇ is Gly or Ser, the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₈: Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH₂.

8. The GLP-1 compound of claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 7 (SEQ ID NO:7)
His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Gly-Pro-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈-Xaa₄₉-Xaa₅₀-Xaa₅₁

Formula 7 (SEQ ID NO:7)

Wherein:

Xaa₃₈ is: Ser, Pro, or His;

Xaa₃₉ is: Ser, Arg, Thr, Trp, or Lys;

Xaa₄₀ is: Ser or Gly;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, or Gly;

Xaa₄₂ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, Pro, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₈ is: Gly, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₉ is: Pro, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₅₀ is: Ser, His, Ser-NH₂, His-NH₂, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; and

Xaa₅₁ is: L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; wherein said extended GLP-1 peptide contains a single L-Cys, D-Cys, homocysteine, or penicillamine which occurs at one of Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, Xaa₅₀, or Xaa₅₁ said GLP-1 is modified at said single L-Cys, D-Cys, homocysteine, or penicillamine; and provided that if Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, or Xaa₅₀, is absent each amino acid downstream is absent.

9. The GLP-1 compound of Claim 1, said GLP-1 peptide having the amino acid sequence of formula 8 (SEQ ID NO:8)

Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Lys-Gly-Arg-Lys

Formula 8 (SEQ ID NO:8)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu; and

Xaa₃₃ is: Val, or Ile;

wherein said GLP-1 peptide is modified at Lys³⁷; and,

provided that the GLP-1 compound does not have the sequence of GLP-1(7-37)OH, GLP-1(7-36)-NH₂, Gly⁸-GLP-1(7-37)OH, Gly⁸-GLP-1(7-36)NH₂, Val⁸-GLP-1(7-37)OH, Val⁸-GLP-1(7-36)NH₂, Leu⁸-GLP-1(7-37)OH, Leu⁸-GLP-1(7-

36)NH₂, Ile⁸-GLP-1(7-37)OH, Ile⁸-GLP-1(7-36)NH₂, Ser⁸-GLP-1(7-37)OH, Ser⁸-GLP-1(7-36)NH₂, Thr⁸-GLP-1(7-37)OH, Thr⁸-GLP-1(7-36)NH₂, Val⁸-Tyr¹²-GLP-1(7-37)OH, Val⁸-Tyr¹²-GLP-1(7-36)NH₂, Val⁸-Tyr¹⁶-GLP-1(7-37)OH, Val⁸-Tyr¹⁶-GLP-1(7-36)NH₂, Val⁸-Glu²²-GLP-1(7-37)OH, Val⁸-Glu²²-GLP-1(7-36)NH₂, Gly⁸-Glu²²-GLP-1(7-37)OH, Gly⁸-Glu²²-GLP-1(7-36)NH₂, Val⁸-Asp²²-GLP-1(7-37)OH, Val⁸-Asp²²-GLP-1(7-36)NH₂, Gly⁸-Asp²²-GLP-1(7-37)OH, Val⁸-Lys²²-GLP-1(7-37)OH, Val⁸-Lys²²-GLP-1(7-36)NH₂, Gly⁸-Lys²²-GLP-1(7-37)OH, Gly⁸-Lys²²-GLP-1(7-36)NH₂, Leu⁸-Glu²²-GLP-1(7-37)OH, Leu⁸-Glu²²-GLP-1(7-36)NH₂, Ile⁸-Glu²²-GLP-1(7-37)OH, Ile⁸-Glu²²-GLP-1(7-36)NH₂, Leu⁸-Asp²²-GLP-1(7-37)OH, Leu⁸-Asp²²-GLP-1(7-36)NH₂, Leu⁸-Lys²²-GLP-1(7-37)OH, Leu⁸-Lys²²-GLP-1(7-36)NH₂, Ile⁸-Asp²²-GLP-1(7-37)OH, Ile⁸-Asp²²-GLP-1(7-36)NH₂, Leu⁸-Lys²²-GLP-1(7-37)OH, Leu⁸-Lys²²-GLP-1(7-36)NH₂, Ser⁸-Glu²²-GLP-1(7-37)OH, Ser⁸-Glu²²-GLP-1(7-36)NH₂, Thr⁸-Glu²²-GLP-1(7-37)OH, Thr⁸-Glu²²-GLP-1(7-36)NH₂, Ser⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Asp²²-GLP-1(7-36)NH₂, Thr⁸-Asp²²-GLP-1(7-37)OH, Thr⁸-Asp²²-GLP-1(7-36)NH₂, Asp²²-GLP-1(7-37)OH, Asp²²-GLP-1(7-36)NH₂, Lys²²-GLP-1(7-37)OH, Lys²²-GLP-1(7-36)NH₂, Val⁸-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu²²-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-36)NH₂, Gly⁸-Glu³⁰-GLP-1(7-37)OH, Gly⁸-Glu³⁰-GLP-1(7-36)NH₂, Leu⁸-Glu³⁰-GLP-1(7-37)OH, Leu⁸-Glu³⁰-GLP-1(7-36)NH₂, Ile⁸-Glu³⁰-GLP-1(7-37)OH, Ile⁸-Glu³⁰-GLP-1(7-36)NH₂, Ser⁸-Glu³⁰-GLP-1(7-37)OH, Ser⁸-Glu³⁰-GLP-1(7-36)NH₂, Thr⁸-Glu³⁰-GLP-1(7-37)OH, Thr⁸-Glu³⁰-GLP-1(7-36)NH₂, Val⁸-His³⁷-GLP-1(7-37)OH, Val⁸-His³⁷-GLP-1(7-36)NH₂, Gly⁸-His³⁷-GLP-1(7-37)OH, Gly⁸-His³⁷-GLP-1(7-36)NH₂, Leu⁸-His³⁷-GLP-1(7-37)OH, Leu⁸-His³⁷-GLP-1(7-36)NH₂, Ile⁸-His³⁷-GLP-1(7-37)OH, Ile⁸-His³⁷-GLP-1(7-36)NH₂, Ser⁸-His³⁷-GLP-1(7-37)OH, Ser⁸-His³⁷-GLP-1(7-36)NH₂, Thr⁸-His³⁷-GLP-1(7-37)OH, Thr⁸-His³⁷-GLP-1(7-36)NH₂, Lys³⁷-GLP-1(7-37)OH.

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10 The GLP-1 compound of Claim 1, said GLP-1 peptide having the amino acid sequence of formula 9 (SEQ ID NO:9)

Xaa₇-Xaa₈-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Tyr-Leu-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Xaa₃₃-Lys-Gly-Arg-Lys

Formula 9 (SEO ID NO:9)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa is: Gly, Ala, Val, Leu, Ile, Ser, or Thr.

Xaa₁ is: Val Phe Tyr or Trp

Xaa, is: Ser, Tyr, Trp, Phe, Lys, Ile, Leu, or Val;

Xaa₃₃ is: Gly, Glu, Asp, or Lys.

Xaaas is: Ala Val Ile or Leu; and

Xaaa is: Val or Ile.

wherein said GI-P-1 peptide is modified at Lys³⁷; and

Lys²²-GLP-1(7-36)NH₂, Ser⁸-Glu²²-GLP-1(7-37)OH, Ser⁸-Glu²²-GLP-1(7-36)NH₂, Thr⁸-Glu²²-GLP-1(7-37)OH, Thr⁸-Glu²²-GLP-1(7-36)NH₂, Ser⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Asp²²-GLP-1(7-36)NH₂, Thr⁸-Asp²²-GLP-1(7-37)OH, Thr⁸-Asp²²-GLP-1(7-36)NH₂, Ser⁸-Lys²²-GLP-1(7-37)OH, Ser⁸-Lys²²-GLP-1(7-36)NH₂, Thr⁸-Lys²²-GLP-1(7-37)OH, Thr⁸-Lys²²-GLP-1(7-36)NH₂, Glu²²-GLP-1(7-37)OH, Glu²²-GLP-1(7-36)NH₂, Asp²²-GLP-1(7-37)OH, Asp²²-GLP-1(7-36)NH₂, Lys²²-GLP-1(7-37)OH, Lys²²-GLP-1(7-36)NH₂, Val⁸-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu²²-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-36)NH₂, Gly⁸-Glu³⁰-GLP-1(7-37)OH, Gly⁸-Glu³⁰-GLP-1(7-36)NH₂, Leu⁸-Glu³⁰-GLP-1(7-37)OH, Leu⁸-Glu³⁰-GLP-1(7-36)NH₂, Ile⁸-Glu³⁰-GLP-1(7-37)OH, Ile⁸-Glu³⁰-GLP-1(7-36)NH₂, Ser⁸-Glu³⁰-GLP-1(7-37)OH, Ser⁸-Glu³⁰-GLP-1(7-36)NH₂, Thr⁸-Glu³⁰-GLP-1(7-37)OH, Thr⁸-Glu³⁰-GLP-1(7-36)NH₂, Val⁸-His³⁷-GLP-1(7-37)OH, Val⁸-His³⁷-GLP-1(7-36)NH₂, Gly⁸-His³⁷-GLP-1(7-37)OH, Gly⁸-His³⁷-GLP-1(7-36)NH₂, Leu⁸-His³⁷-GLP-1(7-37)OH, Leu⁸-His³⁷-GLP-1(7-36)NH₂, Ile⁸-His³⁷-GLP-1(7-37)OH, Ile⁸-His³⁷-GLP-1(7-36)NH₂, Ser⁸-His³⁷-GLP-1(7-37)OH, Ser⁸-His³⁷-GLP-1(7-36)NH₂, Thr⁸-His³⁷-GLP-1(7-37)OH, Thr⁸-His³⁷-GLP-1(7-36)NH₂, Lys³⁷-GLP-1(7-37)OH.

11. The GLP-1 compound of Claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 10 (SEQ ID NO:10)
- Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-Xaa₃₅-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈

Formula 10 (SEQ ID NO:10)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu;

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, Ser, or Lys;

Xaa₃₈ is: Ser, Pro, His, Lys, NH₂;

Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, NH₂, or is absent;

Xaa₄₀ is: Ser, Gly, Lys, NH₂, or is absent;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, NH₂, or is absent;

Xaa₄₂ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, NH₂, or is absent; and

Xaa₄₈ is: Lys, NH₂, or is absent;

wherein said extended GLP-1 peptide is modified at a single Lys which occurs at one of Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, or Xaa₄₈; and provided that if Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent and further provided that the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₆: Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH₂.

12. The GLP-1 compound of Claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 11 (SEQ ID NO:11)
- Xaa₇-Xaa₈-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Xaa₁₆-Ser-Ser-Tyr-Lys-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈

Formula 11 (SEQ ID NO:11)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, Ser, or Lys;

Xaa₃₈ is: Ser, Pro, His, Lys, NH₂, or is absent;

Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, NH₂, or is absent;

Xaa₄₀ is: Ser, Gly, Lys, NH₂, or is absent;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, NH₂, or is absent;

Xaa₄₂ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, NH₂, or is absent; and

Xaa₄₈ is: Lys, NH₂, or is absent;

wherein said extended GLP-1 peptide is modified at a single Lys which occurs at one of Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇,

or Xaa₄₈; and provided that if Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent and further provided that the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₆: Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH₂.

13. The GLP-1 compound of Claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 12 (SEQ ID NO:12)
Xaa₇-Xaa₈-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Lys-Glu-Xaa₂₂-
Gln-Ala-Xaa₂₅-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Xaa₃₃-Lys-Gly-Gly-Pro-
Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈
Formula 12 (SEQ ID NO:12)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;
Xaa₈ is: Gly, Val, Leu, Ile, Ser, or Thr;
Xaa₂₂ is: Gly, Glu, Asp, or Lys;
Xaa₂₅ is: Ala, Val, Ile, or Leu;
Xaa₃₃ is: Val or Ile;
Xaa₃₈ is: Ser, Pro, His, Lys, NH₂, or is absent;
Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, NH₂, or is absent;
Xaa₄₀ is: Ser, Gly, Lys, NH₂, or is absent;
Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, NH₂, or is absent;
Xaa₄₂ is: Pro, Ala, Lys, NH₂, or is absent;
Xaa₄₃ is: Pro, Ala, Lys, NH₂, or is absent;
Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, or is absent;
Xaa₄₅ is: Ser, His, Pro, Lys, Arg, NH₂, or is absent;
Xaa₄₆ is: His, Ser, Arg, Lys, NH₂, or is absent;
Xaa₄₇ is: His, Ser, Arg, Lys, NH₂, or is absent; and
Xaa₄₈ is: Lys, NH₂, or is absent;

wherein said extended GLP-1 peptide is modified at a single Lys which occurs at one of Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, or Xaa₄₈; and provided that if Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent.

14. The GLP-1 compound of Claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 13 (SEQ ID NO:13)
Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-
Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-
Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-
Xaa₄₆-Xaa₄₇-Xaa₄₈-Xaa₄₉-Xaa₅₀- Xaa₅₁
Formula 13 (SEQ ID NO:13)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;
Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;
Xaa₁₂ is: Phe, Trp, or Tyr;
Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;
Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;
Xaa₁₉ is: Tyr, Trp, or Phe;
Xaa₂₀ is: Leu, Phe, Tyr, or Trp;
Xaa₂₂ is: Gly, Glu, Asp, or Lys;
Xaa₂₅ is: Ala, Val, Ile, or Leu;
Xaa₂₇ is: Glu, Ile, or Ala;
Xaa₃₀ is: Ala or Glu
Xaa₃₃ is: Val or Ile;
Xaa₃₄ is: Lys, Asp, Arg, or Glu;
Xaa₃₆ is: Gly, Pro, or Arg;
Xaa₃₇ is: Gly, Pro, or Ser;
Xaa₃₈ is: Ser, Pro, or His;
Xaa₃₉ is: Ser, Arg, Thr, Trp, or Lys;

Xaa₄₀ is: Ser or Gly;
Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, or Gly;
Xaa₄₂ is: Pro, Ala, Lys, NH₂, or is absent;
Xaa₄₃ is: Pro, Ala, Lys, NH₂, or is absent;
Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, or is absent;
Xaa₄₅ is: Ser, His, Pro, Lys, Arg, NH₂, or is absent;
Xaa₄₆ is: His, Ser, Arg, Lys, NH₂, or is absent;
Xaa₄₇ is: His, Ser, Arg, Lys, NH₂, or is absent; and
Xaa₄₈ is: Lys, NH₂, or is absent;
Xaa₄₉ is: Pro, His, Lys, NH₂, or is absent;
Xaa₅₀ is: Ser, His, Lys, NH₂, or is absent; and
Xaa₅₁ is: Lys, NH₂, or is absent;
wherein said extended GLP-1 peptide is modified at a single Lys which occurs at one of Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, Xaa₅₀ or Xaa₅₁; and provided that if Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, or Xaa₅₀, is absent each amino acid downstream is absent.

15. The GLP-1 compound of Claim 1, wherein said GLP-1 peptide is an extended GLP-1 peptide having the amino acid sequence of formula 14 (SEQ ID NO:14)
His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Gly-Pro-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈-Xaa₄₉-Xaa₅₀-Xaa₅₁

Formula 14 (SEQ ID NO:14)

Wherein:

Xaa₃₈ is: Ser, Pro, or His;
Xaa₃₉ is: Ser, Arg, Thr, Trp, or Lys;
Xaa₄₀ is: Ser or Gly;
Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, or Gly;
Xaa₄₂ is: Pro, Ala, Lys, NH₂, or is absent;
Xaa₄₃ is: Pro, Ala, Lys, NH₂, or is absent;
Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, or is absent;

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Xaa₄₅ is: Ser, His, Pro, Lys, Arg, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, NH₂, or is absent; and

Xaa₄₈ is: Lys, NH₂, or is absent;

Xaa₄₉ is: Pro, His, Lys, NH₂, or is absent;

Xaa₅₀ is: Ser, His, Lys, NH₂, or is absent; and

Xaa₅₁ is: Lys, NH₂, or is absent;

wherein said extended GLP-1 peptide is modified at a single Lys which occurs at one of Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, Xaa₅₀, or Xaa₅₁; and provided that if Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, or Xaa₅₀, is absent each amino acid downstream is absent.

16. The GLP-1 compound of any of claims 1-15 wherein said reactive group is an activated disulfide bond group.

17. The GLP-1 compound of any of claims 1-15 wherein said reactive group is an S-sulfonate.

18. A GLP-1 compound comprising a GLP-1 peptide modified with a reactive group that reacts with an amino group, a hydroxyl group, or a thiol group on a blood component to form a covalent bond, wherein said reactive group is selected from the group consisting of a succinimidyl group and a maleimido group, said GLP-1 peptide having the amino acid sequence of formula 15 (SEQ ID NO:15)

Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Lys-Gly-Arg-Xaa₃₇

Formula 15 (SEQ ID NO:15)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;
 Xaa₁₂ is: Phe, Trp, or Tyr;
 Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;
 Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;
 Xaa₁₉ is: Tyr, Trp, or Phe;
 Xaa₂₀ is: Leu, Phe, Tyr, or Trp;
 Xaa₂₂ is: Gly, Glu, Asp, Lys;
 Xaa₂₅ is: Ala, Val, Ile, or Leu;
 Xaa₂₇ is: Glu, Ile, or Ala;
 Xaa₃₀ is: Ala or Glu
 Xaa₃₃ is: Val, or Ile; and
 Xaa₃₇ is: Gly, His, Lys, or NH₂, or is absent,

provided that the GLP-1 compound does not have the sequence of GLP-1(7-37)OH, GLP-1(7-36)-NH₂, Gly⁸-GLP-1(7-37)OH, Gly⁸-GLP-1(7-36)NH₂, Val⁸-GLP-1(7-37)OH, Val⁸-GLP-1(7-36)NH₂, Leu⁸-GLP-1(7-37)OH, Leu⁸-GLP-1(7-36)NH₂, Ile⁸-GLP-1(7-37)OH, Ile⁸-GLP-1(7-36)NH₂, Ser⁸-GLP-1(7-37)OH, Ser⁸-GLP-1(7-36)NH₂, Thr⁸-GLP-1(7-37)OH, Thr⁸-GLP-1(7-36)NH₂, Val⁸-Tyr¹²-GLP-1(7-36)NH₂, Val⁸-Tyr¹⁶-GLP-1(7-37)OH, Val⁸-Tyr¹⁶-GLP-1(7-36)NH₂, Val⁸-Glu²²-GLP-1(7-37)OH, Val⁸-Glu²²-GLP-1(7-36)NH₂, Gly⁸-Glu²²-GLP-1(7-37)OH, Gly⁸-Glu²²-GLP-1(7-36)NH₂, Val⁸-Asp²²-GLP-1(7-37)OH, Val⁸-Asp²²-GLP-1(7-36)NH₂, Gly⁸-Asp²²-GLP-1(7-36)NH₂, Val⁸-Lys²²-GLP-1(7-37)OH, Val⁸-Lys²²-GLP-1(7-36)NH₂, Gly⁸-Lys²²-GLP-1(7-37)OH, Gly⁸-Lys²²-GLP-1(7-36)NH₂, Leu⁸-Glu²²-GLP-1(7-37)OH, Leu⁸-Glu²²-GLP-1(7-36)NH₂, Ile⁸-Glu²²-GLP-1(7-37)OH, Ile⁸-Glu²²-GLP-1(7-36)NH₂, Leu⁸-Asp²²-GLP-1(7-37)OH, Leu⁸-Asp²²-GLP-1(7-36)NH₂, Ile⁸-Asp²²-GLP-1(7-37)OH, Ile⁸-Asp²²-GLP-1(7-36)NH₂, Leu⁸-Lys²²-GLP-1(7-36)NH₂, Ile⁸-Lys²²-GLP-1(7-37)OH, Ile⁸-Lys²²-GLP-1(7-36)NH₂, Ser⁸-Glu²²-GLP-1(7-37)OH, Ser⁸-Glu²²-GLP-1(7-36)NH₂, Thr⁸-Glu²²-GLP-1(7-37)OH, Thr⁸-Glu²²-GLP-1(7-36)NH₂, Ser⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Asp²²-GLP-1(7-36)NH₂, Thr⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Lys²²-GLP-1(7-37)OH, Ser⁸-Lys²²-GLP-1(7-

36)NH₂, Thr⁸-Lys²²-GLP-1(7-37)OH, Thr⁸-Lys²²-GLP-1(7-36)NH₂, Glu²²-GLP-1(7-37)OH, Glu²²-GLP-1(7-36)NH₂, Asp²²-GLP-1(7-37)OH, Asp²²-GLP-1(7-36)NH₂, Lys²²-GLP-1(7-37)OH, Lys²²-GLP-1(7-36)NH₂, Val⁸-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu²²-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-36)NH₂, Gly⁸-Glu³⁰-GLP-1(7-37)OH, Gly⁸-Glu³⁰-GLP-1(7-36)NH₂, Leu⁸-Glu³⁰-GLP-1(7-37)OH, Leu⁸-Glu³⁰-GLP-1(7-36)NH₂, Ile⁸-Glu³⁰-GLP-1(7-37)OH, Ile⁸-Glu³⁰-GLP-1(7-36)NH₂, Ser⁸-Glu³⁰-GLP-1(7-37)OH, Ser⁸-Glu³⁰-GLP-1(7-36)NH₂, Thr⁸-Glu³⁰-GLP-1(7-37)OH, Thr⁸-Glu³⁰-GLP-1(7-36)NH₂, Val⁸-His³⁷-GLP-1(7-37)OH, Val⁸-His³⁷-GLP-1(7-36)NH₂, Gly⁸-His³⁷-GLP-1(7-37)OH, Gly⁸-His³⁷-GLP-1(7-36)NH₂, Leu⁸-His³⁷-GLP-1(7-37)OH, Leu⁸-His³⁷-GLP-1(7-36)NH₂, Ile⁸-His³⁷-GLP-1(7-37)OH, Ile⁸-His³⁷-GLP-1(7-36)NH₂, Ser⁸-His³⁷-GLP-1(7-37)OH, Ser⁸-His³⁷-GLP-1(7-36)NH₂, Thr⁸-His³⁷-GLP-1(7-37)OH, Thr⁸-His³⁷-GLP-1(7-36)NH₂, Lys³⁷-GLP-1(7-37)OH.

19. The GLP-1 compound of Claim 18, wherein Xaa₃₇ of said GLP-1 peptide is Lys and said GLP-1 peptide is modified at Xaa₃₇.
20. A GLP-1 compound comprising an extended GLP-1 peptide modified with a reactive group that reacts with an amino group, a hydroxyl group, or a thiol group on a blood component to form a covalent bond, wherein said reactive group is selected from the group consisting of a succinimidyl group and a maleimido group, said extended GLP-1 peptide having the amino acid sequence of formula 10 (SEQ ID NO:10)

Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈

Formula 10 (SEQ ID NO:10)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu; Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, Ser, or Lys;

Xaa₃₈ is: Ser, Pro, His, or Lys;

Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, NH₂, or is absent;

Xaa₄₀ is: Ser, Gly, Lys, NH₂, or is absent;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, Lys, NH₂, or is absent;

Xaa₄₂ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, NH₂ or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, NH₂ or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, NH₂ or is absent; and

Xaa₄₈ is Lys, NH₂, or is absent;

provided that if Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent and further provided that the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₆: Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH₂.

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21. The GLP-1 compound of Claim 20, wherein said GLP-1 peptide is modified at a Lys, and said Lys occurs at either Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, or Xaa₄₈.
22. A GLP-1 compound comprising an extended GLP-1 peptide modified with a reactive group that reacts with an amino group, a hydroxyl group, or a thiol group on a blood component to form a covalent bond, wherein said reactive group is selected from the group consisting of a succinimidyl group and a maleimido group, said extended GLP-1 peptide having the amino acid sequence of formula 13 (SEQ ID NO:13)

Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈-Xaa₄₉-Xaa₅₀-Xaa₅₁

Formula 13 (SEQ ID NO:13)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, or Ser;

Xaa₃₈ is: Ser, Pro, or His;

Xaa₃₉ is: Ser, Arg, Thr, Trp, or Lys;

Xaa₄₀ is: Ser or Gly;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, or Gly;

Xaa₄₂ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, Lys, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, NH₂, or is absent; and

Xaa₄₈ is: Lys, NH₂, or is absent;

Xaa₄₉ is: Pro, His, Lys, NH₂, or is absent;

Xaa₅₀ is: Ser, His, Lys, NH₂, or is absent; and

Xaa₅₁ is: Lys, NH₂, or is absent;

wherein said extended GLP-1 peptide is modified at a single Lys which occurs at one of Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, Xaa₅₀, or Xaa₅₁; and provided that if Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, or Xaa₅₀, is absent each amino acid downstream is absent.

23. The GLP-1 compound of Claim 22, wherein said GLP-1 peptide is modified at a Lys, and said Lys occurs at either Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, Xaa₅₀ or Xaa₅₁.
24. The GLP-1 compound as in any of claims 12-23 wherein said reactive group is a succinimidyl group.
25. The GLP-1 compound as in any of claims 12-23 wherein said reactive group is a maleimido group.

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26. A GLP-1 compound comprising a GLP-1 peptide modified with a reactive group that reacts with a thiol group on a blood component to form a covalent bond, wherein said reactive group is a succinimidyl group, said GLP-1 peptide having the amino acid sequence of formula 1 (SEQ ID NO:1)

Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Lys-Gly-Arg-Xaa₃₇

Formula 1 (SEQ ID NO:1)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu;

Xaa₃₃ is: Val, or Ile; and

Xaa₃₇ is: L-Cys, D-Cys, homocysteine, or penicillamine;

wherein said GLP-1 peptide is modified at Xaa₃₇; and

provided that the GLP-1 compound does not have the sequence of GLP-1(7-37)OH, GLP-1(7-36)-NH₂, Gly⁸-GLP-1(7-37)OH, Gly⁸-GLP-1(7-36)NH₂, Val⁸-GLP-1(7-37)OH, Val⁸-GLP-1(7-36)NH₂, Leu⁸-GLP-1(7-37)OH, Leu⁸-GLP-1(7-36)NH₂, Ile⁸-GLP-1(7-37)OH, Ile⁸-GLP-1(7-36)NH₂, Ser⁸-GLP-1(7-37)OH, Ser⁸-GLP-1(7-36)NH₂, Thr⁸-GLP-1(7-37)OH, Thr⁸-GLP-1(7-36)NH₂, Val⁸-Tyr¹²-GLP-1(7-37)OH, Val⁸-Tyr¹²-GLP-1(7-36)NH₂, Val⁸-Tyr¹⁶-GLP-1(7-37)OH, Val⁸-Tyr¹⁶-GLP-1(7-36)NH₂, Val⁸-Glu²²-GLP-1(7-37)OH, Val⁸-Glu²²-GLP-1(7-

36)NH₂, Gly⁸-Glu²²-GLP-1(7-37)OH, Gly⁸-Glu²²-GLP-1(7-36)NH₂, Val⁸-Asp²²-GLP-1(7-37)OH, Val⁸-Asp²²-GLP-1(7-36)NH₂, Gly⁸-Asp²²-GLP-1(7-37)OH, Gly⁸-Asp²²-GLP-1(7-36)NH₂, Val⁸-Lys²²-GLP-1(7-37)OH, Val⁸-Lys²²-GLP-1(7-36)NH₂, Gly⁸-Lys²²-GLP-1(7-37)OH, Gly⁸-Lys²²-GLP-1(7-36)NH₂, Leu⁸-Glu²²-GLP-1(7-37)OH, Leu⁸-Glu²²-GLP-1(7-36)NH₂, Ile⁸-Glu²²-GLP-1(7-37)OH, Ile⁸-Glu²²-GLP-1(7-36)NH₂, Leu⁸-Asp²²-GLP-1(7-37)OH, Leu⁸-Asp²²-GLP-1(7-36)NH₂, Ile⁸-Asp²²-GLP-1(7-37)OH, Ile⁸-Asp²²-GLP-1(7-36)NH₂, Leu⁸-Lys²²-GLP-1(7-37)OH, Leu⁸-Lys²²-GLP-1(7-36)NH₂, Ile⁸-Lys²²-GLP-1(7-37)OH, Ile⁸-Lys²²-GLP-1(7-36)NH₂, Ser⁸-Glu²²-GLP-1(7-37)OH, Ser⁸-Glu²²-GLP-1(7-36)NH₂, Thr⁸-Glu²²-GLP-1(7-37)OH, Thr⁸-Glu²²-GLP-1(7-36)NH₂, Ser⁸-Asp²²-GLP-1(7-37)OH, Ser⁸-Asp²²-GLP-1(7-36)NH₂, Thr⁸-Asp²²-GLP-1(7-37)OH, Thr⁸-Asp²²-GLP-1(7-36)NH₂, Ser⁸-Lys²²-GLP-1(7-37)OH, Ser⁸-Lys²²-GLP-1(7-36)NH₂, Thr⁸-Lys²²-GLP-1(7-37)OH, Thr⁸-Lys²²-GLP-1(7-36)NH₂, Glu²²-GLP-1(7-37)OH, Glu²²-GLP-1(7-36)NH₂, Asp²²-GLP-1(7-37)OH, Asp²²-GLP-1(7-36)NH₂, Lys²²-GLP-1(7-37)OH, Lys²²-GLP-1(7-36)NH₂, Val⁸-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu²²-Ala²⁷-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-37)OH, Val⁸-Glu³⁰-GLP-1(7-36)NH₂, Gly⁸-Glu³⁰-GLP-1(7-37)OH, Gly⁸-Glu³⁰-GLP-1(7-36)NH₂, Leu⁸-Glu³⁰-GLP-1(7-37)OH, Leu⁸-Glu³⁰-GLP-1(7-36)NH₂, Ile⁸-Glu³⁰-GLP-1(7-37)OH, Ile⁸-Glu³⁰-GLP-1(7-36)NH₂, Ser⁸-Glu³⁰-GLP-1(7-37)OH, Ser⁸-Glu³⁰-GLP-1(7-36)NH₂, Thr⁸-Glu³⁰-GLP-1(7-37)OH, Thr⁸-Glu³⁰-GLP-1(7-36)NH₂, Val⁸-His³⁷-GLP-1(7-37)OH, Val⁸-His³⁷-GLP-1(7-36)NH₂, Gly⁸-His³⁷-GLP-1(7-37)OH, Gly⁸-His³⁷-GLP-1(7-36)NH₂, Leu⁸-His³⁷-GLP-1(7-37)OH, Leu⁸-His³⁷-GLP-1(7-36)NH₂, Ile⁸-His³⁷-GLP-1(7-37)OH, Ile⁸-His³⁷-GLP-1(7-36)NH₂, Ser⁸-His³⁷-GLP-1(7-37)OH, Ser⁸-His³⁷-GLP-1(7-36)NH₂, Thr⁸-His³⁷-GLP-1(7-37)OH, Thr⁸-His³⁷-GLP-1(7-36)NH₂.

27. A GLP-1 compound comprising an extended GLP-1 peptide modified with a reactive group that reacts with a thiol group on a blood component to form a covalent bond, wherein said reactive group is a succinimidyl group, said extended GLP-1 peptide having the amino acid sequence of formula 3 (SEQ ID NO:3)

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Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-
Glu-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-
Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-
Xaa₄₆-Xaa₄₇-Xaa₄₈

Formula 3 (SEQ ID NO:3)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, Ser, L-Cys, D-Cys, homocysteine, or penicillamine;

Xaa₃₈ is: Ser, Pro, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂;

Xaa₃₉ is: Ser, Arg, Thr, Trp, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₀ is: Ser, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₂ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

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Xaa₄₄ is: Pro, Ala, Arg, Lys, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; and

Xaa₄₈ is: L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; wherein said extended GLP-1 peptide contains a single L-Cys, D-Cys, homocysteine, or penicillamine which occurs at one of Xaa₃₇, Xaa₃₈, Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, or Xaa₄₈, said GLP-1 is modified at said single L-Cys, D-Cys, homocysteine, or penicillamine; and provided that if Xaa₃₉, Xaa₄₀, Xaa₄₁, Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, or Xaa₄₇ is absent each amino acid downstream is absent and further provided that the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₆: Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH₂.

28. A GLP-1 compound comprising an extended GLP-1 peptide modified with a reactive group that reacts with a thiol group on a blood component to form a covalent bond, wherein said reactive group is a succinimidyl group, said extended GLP-1 peptide having the amino acid sequence of formula 6 (SEQ ID NO:6)
- Xaa₇-Xaa₈-Glu-Gly-Thr-Xaa₁₂-Thr-Ser-Asp-Xaa₁₆-Ser-Xaa₁₈-Xaa₁₉-Xaa₂₀-Glut-Xaa₂₂-Gln-Ala-Xaa₂₅-Lys-Xaa₂₇-Phe-Ile-Xaa₃₀-Trp-Leu-Xaa₃₃-Xaa₃₄-Gly-Xaa₃₆-Xaa₃₇-Xaa₃₈-Xaa₃₉-Xaa₄₀-Xaa₄₁-Xaa₄₂-Xaa₄₃-Xaa₄₄-Xaa₄₅-Xaa₄₆-Xaa₄₇-Xaa₄₈-Xaa₄₉-Xaa₅₀-Xaa₅₁

Formula 6 (SEQ ID NO:6)

wherein:

Xaa₇ is: L-histidine, D-histidine, desamino-histidine, 2-amino-histidine, β -hydroxy-histidine, homohistidine, α -fluoromethyl-histidine, or α -methyl-histidine;

Xaa₈ is: Ala, Gly, Val, Leu, Ile, Ser, or Thr;

Xaa₁₂ is: Phe, Trp, or Tyr;

Xaa₁₆ is: Val, Trp, Ile, Leu, Phe, or Tyr;

Xaa₁₈ is: Ser, Trp, Tyr, Phe, Lys, Ile, Leu, Val;

Xaa₁₉ is: Tyr, Trp, or Phe;

Xaa₂₀ is: Leu, Phe, Tyr, or Trp;

Xaa₂₂ is: Gly, Glu, Asp, or Lys;

Xaa₂₅ is: Ala, Val, Ile, or Leu;

Xaa₂₇ is: Glu, Ile, or Ala;

Xaa₃₀ is: Ala or Glu

Xaa₃₃ is: Val or Ile;

Xaa₃₄ is: Lys, Asp, Arg, or Glu;

Xaa₃₆ is: Gly, Pro, or Arg;

Xaa₃₇ is: Gly, Pro, or Ser;

Xaa₃₈ is: Ser, Pro, or His;

Xaa₃₉ is: Ser, Arg, Thr, Trp, or Lys;

Xaa₄₀ is: Ser or Gly;

Xaa₄₁ is: Ala, Asp, Arg, Glu, Lys, or Gly;

Xaa₄₂ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₃ is: Pro, Ala, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₄ is: Pro, Ala, Arg, Lys, His, NH₂, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₅ is: Ser, His, Pro, Lys, Arg, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₆ is: His, Ser, Arg, Lys, Pro, Gly, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₇ is: His, Ser, Arg, Lys, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₈ is: Gly, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₄₉ is: Pro, His, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent;

Xaa₅₀ is: Ser, His, Ser-NH₂, His-NH₂, L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; and

Xaa₅₁ is: L-Cys, D-Cys, homocysteine, penicillamine, NH₂, or is absent; wherein said extended GLP-1 peptide contains a single L-Cys, D-Cys, homocysteine, or penicillamine which occurs at one of Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, Xaa₅₀, or Xaa₅₁ said GLP-1 is modified at said single L-Cys, D-Cys, homocysteine, or penicillamine; and provided that if Xaa₄₂, Xaa₄₃, Xaa₄₄, Xaa₄₅, Xaa₄₆, Xaa₄₇, Xaa₄₈, Xaa₄₉, or Xaa₅₀, is absent each amino acid downstream is absent and further provided that if Xaa₃₆ is Arg and Xaa₃₇ is Gly or Ser, the GLP-1 peptide does not have the following C-terminal amino acid extension beginning at Xaa₃₈: Ser-Ser-Gly-Ala-Pro-Pro-Ser-NH₂.

29. The GLP-1 compound of any of Claims 2, 3, 9, 10, 18, 19, or 26 provided that the GLP-1 compound does not differ from GLP-1(7-37)OH or GLP-1(7-36)NH₂ by more than 5 amino acids.
30. The GLP-1 compound of Claim 29 provided that the GLP-1 compound does not differ from GLP-1(7-37)OH or GLP-1(7-36)NH₂ by more than 4 amino acids.
31. The GLP-1 compound of Claim 30 provided that the GLP-1 compound does not differ from GLP-1(7-37)OH or GLP-1(7-36)NH₂ by more than 3 amino acids.
32. The GLP-1 compound of any of Claims 4-8, 11-15, 20-23, 27 or 28 wherein the first 31 amino acids of the peptide do not differ from GLP-1(7-37) by more than 6 amino acids.
33. The GLP-1 compound of Claim 32 wherein the first 31 amino acids of the peptide do not differ from GLP-1(7-37) by more than 5 amino acids.
34. The GLP-1 compound of Claim 33 wherein the first 31 amino acids of the peptide do not differ from GLP-1(7-37) by more than 4 amino acids.

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35. The GLP-1 compound of Claim 33 wherein the first 31 amino acids of the peptide do not differ from GLP-1(7-37) by more than 3 amino acids.
36. A conjugate comprising a GLP-1 compound of any of claims 1 through 35 covalently bonded ex vivo to a blood component.
37. A conjugate comprising a GLP-1 compound of any of claims 1 through 35 covalently bonded ex vivo to a blood serum albumin.
38. A method for extending the in vivo half-life of a GLP-1 compound as claimed in any of claims 1 through 35, comprising reacting said reactive group of said pharmaceutical composition with a thiol group on a blood component in vivo.
39. A method for extending the in vivo half-life of a GLP-1 compound as claimed in any of claims 1 through 35, comprising reacting said reactive group of said pharmaceutical composition with a thiol group on blood serum albumin in vivo.
40. A method of stimulating the GLP-1 receptor in a subject in need of such stimulation, said method comprising the step of administering to the subject an effective amount of the GLP-1 compound of any one of Claims 1 through 35.
41. The method of Claim 40 wherein the subject is being treated for non-insulin dependent diabetes.
42. The method of Claim 40 wherein the subject is being treated prophylactically for non insulin dependent diabetes.
43. The method of Claim 40 wherein the subject is being treated for obesity.

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44. The method of Claim 40 wherein the subject is being treated for stroke, myocardial infarction, stroke, stress-induced hyperglycemia, or irritable bowel syndrome.
45. The use of a GLP-1 compound of any one of Claims 1 through 35 in the manufacture of a medicament for the treatment of non-insulin dependent diabetes, obesity, stroke, myocardial infarction, stress-induced hyperglycemia, or irritable bowel syndrome.
46. The use of Claim 45 wherein the medicament is used to treat non-insulin dependent diabetes.
47. The use of claim 45 wherein the medicament is used to treat obesity.